



TITLE:

<Division of Synthetic Chemistry>Synthetic Organic Chemistry

AUTHOR(S):

CITATION:

<Division of Synthetic Chemistry>Synthetic Organic Chemistry. ICR Annual Report 2015, 22: 8-9

ISSUE DATE:

2015

URL:

<http://hdl.handle.net/2433/209877>

RIGHT:

Division of Synthetic Chemistry – Synthetic Organic Chemistry –

<http://www.fos.kuicr.kyoto-u.ac.jp/EnglishTop/English.top.html>



Prof
KAWABATA, Takeo
(D Pharm Sc)



Assoc Prof
FURUTA, Takumi
(D Pharm Sc)



Assist Prof
YOSHIMURA, Tomoyuki
(D Pharm Sc)



Assist Prof
UEDA, Yoshihiro
(D Pharm Sc)



Techn Staff
FUJIIHASHI, Akiko



PD
HARISADHAN, Ghosh
(Ph D)



PD
YELLA, Ramesh
(Ph D)

Researcher

NOBUTA, Tomoya (D Pharm Sc)

Students

BABA, Tomonori (D4)
YANAGI, Masanori (D4)
TAKEUCHI, Hironori (D3)
LU, Wenjie (D3)
TSUDA, Ayumi (D3)
HYAKUTAKE, Ryuichi (D3)
HIRATA, Atsushi (D3)
KASAMATSU, Koji (D2)
KURIBAYASHI, Toshifumi (D2)
NAKAGAWA, Akihiro (D2)
HAYASAKA, Manami (D2)
ARAI, Kenta (D1)
OTSUKI, Haruka (D1)

TANAKA, Yuya (M2)
FUJIMORI, Yusuke (M2)
NISHIJIMA, Hideyuki (M2)
ORITA, Takuya (M1)
GONDOH, Naruhiro (M1)
SHIBAYAMA, Hiromitsu (M1)
SHIMODA, Shotaro (M1)
MATAYOSHI, Aki (M1)
SHIMMIYA, Ruri (UG)
NAGAISHI, Masaru (UG)
NINOMIYA, Ryo (UG)
YAMAMOTO, Satoru (UG)

Scope of Research

The research interests of this laboratory include the development of advanced molecular transformation, total synthesis of biologically active products, and molecular recognition. Programs are active in the following areas: 1) asymmetric alkylation of carbonyl compounds based on “memory of chirality”, 2) organocatalysis for fine organic syntheses, 3) synthesis of unusual amino acids and nitrogen heterocycles, 4) regioselective functionalization of carbohydrates, and 5) the structural and functional investigation of heterochiral oligomers.

KEYWORDS

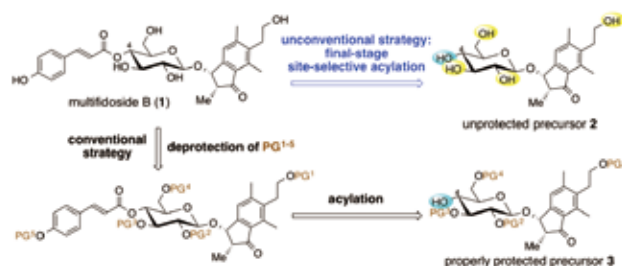
Organocatalysis
Regioselective Functionalization
Dynamic Chirality
Unusual Amino Acid
Molecular Recognition

Selected Publications

- Kawabata, T.; Moriyama, K.; Kawakami, S.; Tsubaki, K., Powdered KOH in DMSO: An Efficient Base for Asymmetric Cyclization via Memory of Chirality at Ambient Temperature, *J. Am. Chem. Soc.*, **130**, 4153-4157 (2008).
- Kawabata, T.; Jiang, C.; Hayashi, K.; Tsubaki, K.; Yoshimura, T.; Majumdar, S.; Sasamori, T.; Tokitoh, N., Axially Chiral Binaphthyl Surrogates with an Inner N-H-N Hydrogen Bond, *J. Am. Chem. Soc.*, **131**, 54-55 (2009).
- Yoshida, K.; Furuta, T.; Kawabata, T., Organocatalytic Chemoselective Monoacylation of 1,n-Linear Diol, *Angew. Chem. Int. Ed.*, **50**, 4888-4892 (2011).
- Hamada, S.; Furuta, T.; Wada, Y.; Kawabata, T., Chemoselective Oxidation by Electronically Tuned Nitroxyl Radical Catalysts, *Angew. Chem. Int. Ed.*, **52**, 8093-8097 (2013).
- Tomohara, K.; Yoshimura, T.; Hyakutake, R.; Yang, P.; Kawabata, T., Asymmetric α -Arylation of Amino Acid Derivatives by Clayden Rearrangement of Ester Enolates via Memory of Chirality, *J. Am. Chem. Soc.*, **135**, 13294-13297 (2013).
- Yoshimura, T.; Tomohara, K.; Kawabata, T., Asymmetric Induction via Short-Lived Chiral Enolates with Chiral C-O Axis, *J. Am. Chem. Soc.*, **135**, 7102-7105 (2013).
- Takeuchi, H.; Mishiro, K.; Ueda, Y.; Fujimori, Y.; Furuta, T.; Kawabata, T., Total Synthesis of Ellagitannins via Regioselective Sequential Functionalization of Unprotected Glucose, *Angew. Chem. Int. Ed.*, **54**, 6177-6180 (2015).
- Ueda, Y.; Furuta, T.; Kawabata, T., Final-Stage Site-Selective Acylation for the Total Syntheses of Multifidosides A-C, *Angew. Chem. Int. Ed.*, **54**, 11966-11970 (2015).

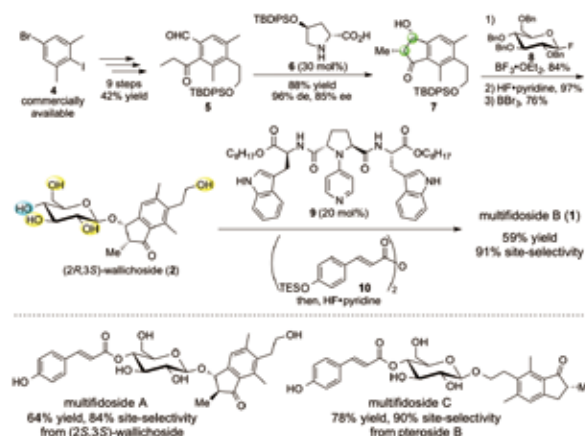
An Unconventional Retrosynthesis of Acylated Natural Glycosides: Final-stage Site-selective Acylation of Unprotected Glycosides

Several hundreds of acylated glycosides such as phenylethanoid glycosides and ellagitannins exist in nature. Some of them show potent biological activities including antiviral, antitumor, and antiallergic activities, and have attracted interest for synthesis. Multifidosides A-C, isolated from whole plants used in traditional Chinese medicine, possess a *p*-coumaroyl group at C(4)-OH of the glucopyranose moiety. Properly protected precursor **3** with free C(4)-OH is a rational precursor for the synthesis of multifidoside B (**1**) based on the conventional protection/deprotection strategy. In contrast, we propose an unconventional strategy based on final-stage site-selective acylation: the *p*-coumaroyl group can be introduced directly onto the C(4)-OH of the unprotected precursor **2** at the final step of total synthesis. The expected advantages of the proposed strategy would be: 1) streamlining for fewer steps for the total synthesis and 2) avoidance of the risks of the undesired side reactions during the removal of the protecting groups (PGs) at a later stage of the conventional synthetic scheme.



Unprotected precursor **2** was readily prepared by a thirteen-step transformation from commercially available **4**, in which an intramolecular asymmetric aldol reaction of **5** catalyzed by organocatalyst **6** was performed as a key step. As we expected, acylation of **2** promoted by our originally developed organocatalyst **9** took place at the intrinsically less reactive C(4)-OH of the glucopyranose substructure even in the presence of two primary hydroxy groups. Thus, multifidoside C was obtained in one step from the unprotected precursor **2** by the removal of the TES group during the work-up process. Notably, the synthetic route has a one-step conversion from a natural glycoside into another natural glycoside, since **2** is also a naturally occurring glycoside named (2*R*,3*S*)-wallichoside. Similarly, the first total syntheses of multifidosides A and C have been achieved by final-stage site-selective acylation of the precursor natural glycosides, (2*S*,3*S*)-wallichoside and pteroside B, respectively. Considering the predictability and reliability of the site-selective acylation promoted by catalyst **9**, the

proposed strategy could provide a general synthetic route to 4-O-acylglycosides.



Asymmetric α -Arylation of Amino Acid Derivatives by Intramolecular Aryl Migration of Ester Enolates via Memory of Chirality

Asymmetric α -arylation of amino acids has been a challenge in current organic synthesis. We have developed a method for asymmetric α -arylation of amino acid derivatives via intramolecular aryl migration (Clayden rearrangement) of chiral enolates generated from amino acid esters, based on the protocol of memory of chirality. The reaction took place through inversion of configuration via chiral enolate intermediate **A**, whose racemization barrier was ~ 15 kcal/mol at -78 °C. The half-life of racemization of the axially chiral enolate was estimated to be ~ 5 min at -60 °C (reaction temperature). This method provides chiral hydantoins with aryl-substituted tetrasubstituted carbon, potentially useful chiral building blocks in the field of medicinal chemistry, and are structural equivalents to amino acids with aryl-substituted tetrasubstituted carbon.

